

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

Amendment

In the Claims

1. (original) A compound comprising a target specific portion and an effector portion wherein:
  - (i) the target specific portion comprises or consists of a monoclonal antibody having specificity for oncofoetal fibronectin, or a fragment or variant thereof which retains the binding specificity for oncofoetal fibronectin of the parent monoclonal antibody; and
  - (ii) the effector portion comprises or consists of interleukin-12, or a functional fragment or variant thereofcharacterised in the monoclonal antibody having specificity for oncofoetal fibronectin binds to a region of oncofoetal fibronectin other than the ED-B region.
2. (original) A compound according to Claim 1 wherein the target specific portion is capable of binding to an amino acid sequence within the repeat 7 domain of fibronectin.
3. (previously presented) A compound according to Claim 1 wherein the target specific portion is capable of binding an amino acid sequence within the repeat 7 domain of fibronectin.
4. (previously presented) A compound according to Claim 1 wherein the target specific portion is specific for human oncofoetal fibronectin.
5. (previously presented) A compound according to Claim 1 wherein the monoclonal antibody having specificity for oncofoetal fibronectin is a BC1 antibody, or an antibody capable of competing with the binding of a BC1 antibody to oncofoetal fibronectin.

**AMENDMENT AND RESPONSE TO TO RESTRICTION REQUIREMENT**

6. (original) A compound according to Claim 5 wherein the monoclonal antibody having specificity for oncofoetal fibronectin is a BC1 antibody.
7. (previously presented) A compound according to Claim 1 wherein the monoclonal antibody is a human or humanized antibody.
8. (previously presented) A compound according to Claim 6 wherein the compound binds to oncofoetal fibronectin more tightly than the parent monoclonal antibody.
9. (original) A compound according to Claim 8 wherein the compound binds to oncofoetal fibronectin more at least 2-fold tighter than the parent monoclonal antibody.
10. (previously presented) A compound according to Claim 8 wherein the compound binds to oncofoetal fibronectin at least 10-fold tighter than the parent BC1 antibody binds to oncofoetal fibronectin.
11. (previously presented) A compound according to Claim 1 wherein the target specific portion comprises a polypeptide of SEQ ID NO: 1.
12. (previously presented) A compound according to Claim 1 wherein the target specific portion comprises a polypeptide of SEQ ID NO: 2.
13. (previously presented) A compound according to Claim 11 wherein the target specific portion comprises a polypeptide of SEQ ID NO: 1 and a polypeptide SEQ ID NO: 2.
14. (previously presented) A compound according to Claim 1 wherein the target specific portion comprises or consists of an antigen binding fragment of a monoclonal antibody having specificity for oncofoetal fibronectin.

AMENDMENT AND RESPONSE TO TO RESTRICTION REQUIREMENT

15. (original) A compound according to Claim 14 wherein the target specific portion comprises or consists of an antigen binding fragment selected from the group consisting of FAB-like molecules, such as Fab and F(ab')<sub>2</sub>, Fv molecules, disulphide-linked Fv molecules, ScFv molecules and single domain antibodies (dAbs).

16. (previously presented) A compound according to Claim 1 wherein the target specific portion comprises one or more antibody constant regions.

17. (original) A compound according to Claim 16 wherein the one or more antibody constant regions comprises or consists of a CH1 domain.

18. (previously presented) A compound according to Claim 1 further comprising an Fe moiety.

19. (original) A compound according to Claim 18 wherein the Fe moiety is derived from human IgG1.

20. (previously presented) A compound according to Claim 1 wherein the target specific portion comprises or consists of a whole BC1 antibody.

21. (previously presented) A compound according to Claim 1 wherein the effector portion comprises or consists of human interleukin-12, or a functional fragment or variant thereof.

22. (previously presented) A compound according to Claim 1 wherein the effector portion comprises or consists of a single-chain interleukin-12.

**AMENDMENT AND RESPONSE TO TO RESTRICTION REQUIREMENT**

23. (previously presented) A compound according to Claim 22 wherein the single chain IL-12 consists of an IL-12p35 domain and an IL-12p40 domain.

24. (previously presented) A compound according to Claim 23 wherein the IL-12p35 domain is conjugated to the IL-12p40 domain by a disulphide bond.

25. (previously presented) A compound according to Claim 1 wherein the compound is a fusion protein.

26. (previously presented) A compound according to Claim 1 wherein the target specific portion is fused to the effector portion.

27. (original) A compound according to Claim 26 comprising an immunoglobulin heavy chain fused to the effector portion.

28. (original) A compound according to Claim 27 wherein the immunoglobulin heavy chain and the effector portion are joined via a mutated linker sequence.

29. (original) A compound according to Claim 28 wherein the linker comprises or consists of the amino acid sequence ATATPGAA (SEQ ID NO: 5).

30. (previously presented) A compound according to Claim 1 wherein the compound comprises a polypeptide of SEQ ID NO: 6.

31. (previously presented) A compound according to Claim 1 wherein the compound comprises a polypeptide of SEQ ID NO: 7.

32. (previously presented) A compound according to Claim 30 wherein the compound comprises a polypeptide of SEQ ID NO:6 and a polypeptide of SEQ ID NO:7.

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**AMENDMENT AND RESPONSE TO TO RESTRICTION REQUIREMENT**

33. (previously presented) A compound according to Claim 30 further comprising a polypeptide of SEQ ID 4 linked by disulphide bond to the polypeptide of SEQ ID NO:6.

34. (original) A fusion protein comprising antibody V regions directed against oncofoetal fibronectin, an Fe moiety, and an interleukin-12 moiety.

35.- 42. (canceled)

43. (previously presented) A pharmaceutical composition comprising a compound according to Claim 1 and a pharamaceutically acceptable carrier.

44. (original) A pharmaceutical composition according to Claim 43 wherein the composition is suitable for parenteral administration.

45. (previously presented) A compound according to Claim 1 for use in medicine.

46. (canceled)

47. (previously presented) A method of treating a patient with cancer, the method comprising administering a compound according to Claim 1 to said patient.

48. (previously presented) The method according to Claim 47 wherein the mammal is a human.

49. (previously presented) The method according to Claim 47 wherein the patient has a solid tumor.

50. (previously presented) The method according to Claim 47 wherein the cancer is a glioblastoma.

51. (canceled)

U.S.S.N. 10/596,997

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**AMENDMENT AND RESPONSE TO TO RESTRICTION REQUIREMENT**

52. (canceled)